

We claim:

1. A molecular complex which comprises at least four fusion proteins, wherein:

5 (a) two first fusion proteins comprise (i) an immunoglobulin heavy chain, wherein the immunoglobulin heavy chain comprises a variable region, and (ii) an extracellular domain of a first transmembrane polypeptide; and

10 (b) two second fusion proteins comprise (i) an immunoglobulin light chain and (ii) an extracellular domain of a second transmembrane polypeptide; wherein the fusion proteins associate to form the molecular complex, wherein the molecular complex comprises two ligand binding sites, each ligand binding site formed by the extracellular domains of the first and second transmembrane polypeptides, wherein the affinity of the molecular complex for a cognate ligand is increased at least two-fold over a dimeric molecular complex consisting of a first and a second fusion protein.

15 2. The molecular complex of claim 1 wherein the first transmembrane polypeptide is an MHC class II β chain and wherein the second transmembrane polypeptide is an MHC class II α chain.

20 3. The molecular complex of claim 1 wherein the first transmembrane polypeptide is a T cell receptor (TCR) α chain and wherein the second transmembrane polypeptide is a TCR β chain.

4. The molecular complex of claim 1 wherein the immunoglobulin heavy chain is an IgG1 heavy chain.

25 5. The molecular complex of claim 1 wherein the immunoglobulin light chain is an Ig κ chain.

30 6. The molecular complex of claim 1 wherein the first fusion proteins comprise a first peptide linker between the immunoglobulin heavy chain and the extracellular domain of the first transmembrane polypeptide and wherein the second fusion proteins comprise a second peptide linker between the immunoglobulin light chain and the extracellular domain of the second transmembrane polypeptide.

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7. The molecular complex of claim 6 wherein the first peptide linker is GLY-GLY-GLY-THR-SER-GLY (SEQ ID NO:10).
8. The molecular complex of claim 6 wherein the second peptide linker is GLY-SER-LEU-GLY-GLY-SER (SEQ ID NO:11).
- 5 9. The molecular complex of claim 1 wherein antigenic peptides are bound to the ligand binding sites.
- 10 10. The molecular complex of claim 9 wherein an identical antigenic peptide is bound to each antigenic binding site.
- 10 11. The molecular complex of claim 9 wherein the antigenic peptides are passively bound.
12. The molecular complex of claim 9 wherein the antigenic peptides are actively bound.
13. The molecular complex of claim 9 wherein the antigenic peptides are covalently bound.
- 15 14. The molecular complex of claim 1 which is conjugated to a toxin.
- 15 15. The molecular complex of claim 1 which is conjugated to a molecule which stimulates an immune response.
- 20 16. The molecular complex of claim 1 which comprises a pharmaceutically acceptable carrier.
17. A polynucleotide which encodes:
- 25 a first fusion protein comprising (i) an immunoglobulin heavy chain, wherein the immunoglobulin heavy chain comprises a variable region, and (ii) an extracellular domain of a first transmembrane polypeptide of a heterodimeric protein, wherein the immunoglobulin light chain is C-terminal to the extracellular domain of the first transmembrane polypeptide; and
- 30 a second fusion protein comprising (i) an immunoglobulin light chain and (ii) an extracellular domain of a second transmembrane polypeptide of the heterodimeric protein, wherein the immunoglobulin light chain is C-terminal to the extracellular portion of the second transmembrane polypeptide,

wherein the extracellular domains of the first and second transmembrane polypeptides form a ligand binding site.

18. The polynucleotide of claim 18 wherein the polynucleotide further comprises a baculovirus replication system.

5 19. The expression construct of claim 17 wherein the first transmembrane polypeptide is an MHC class II β chain and wherein the second transmembrane polypeptide is an MHC class II α chain.

10 20. The expression construct of claim 17 wherein the first transmembrane polypeptide is a TCR α chain and wherein the second transmembrane polypeptide is a TCR β chain.

15 21. The expression construct of claim 17 wherein the immunoglobulin heavy chain is an IgG1 heavy chain.

22. The expression construct of claim 17 wherein the immunoglobulin light chain is an Ig κ light chain.

15 23. The expression construct of claim 17 wherein the first fusion protein comprises a first peptide linker between the immunoglobulin heavy chain and the extracellular domain of the first transmembrane polypeptide and wherein the second fusion protein comprises a second peptide linker between the immunoglobulin light chain and the extracellular domain of the second transmembrane polypeptide.

20 24. The expression construct of claim 23 wherein the first peptide linker is GLY-GLY-GLY-THR-SER-GLY (SEQ ID NO:10).

25 25. The expression construct of claim 23 wherein the second peptide linker is GLY-SER-LEU-GLY-GLY-SER (SEQ ID NO:11).

26. A host cell comprising at least one expression construct
25 encoding:

30 a first fusion protein comprising (i) an immunoglobulin heavy chain, wherein the immunoglobulin heavy chain comprises a variable region, and (ii) an extracellular domain of a first transmembrane polypeptide of a heterodimeric protein, wherein the immunoglobulin light chain is C-terminal to the extracellular domain of the first transmembrane polypeptide; and

a second fusion protein comprising (i) an immunoglobulin light chain and (ii) an extracellular domain of a second transmembrane polypeptide of the heterodimeric protein, wherein the immunoglobulin light chain is C-terminal to the extracellular portion of the second transmembrane polypeptide,

wherein the extracellular domains of the first and second transmembrane polypeptides form a ligand binding site, wherein the affinity of the molecular complex for a cognate ligand is increased at least two-fold over a dimeric molecular complex consisting of a first and a second fusion protein.

10 27. The host cell of claim 27 wherein a first expression construct
encodes the first fusion protein and wherein a second expression construct
encodes the second fusion protein.

28. A composition comprising a cell in which a molecular complex is bound to the surface of the cell, wherein the molecular complex comprises at least four fusion proteins, wherein:

(a) two first fusion proteins comprise an immunoglobulin heavy chain, wherein the immunoglobulin heavy chain comprises a variable region, and an extracellular portion of a first transmembrane polypeptide; and

(b) two second fusion proteins comprise an immunoglobulin light chain and an extracellular portion of a second transmembrane polypeptide;

wherein the fusion proteins associate to form a molecular complex, wherein the molecular complex comprises two ligand binding sites, each ligand binding site formed by the extracellular domains of the first and second transmembrane polypeptides, wherein the affinity of the molecular complex for a cognate ligand is increased at least two-fold over a dimeric molecular complex consisting of a first and a second fusion protein.

29. The composition of claim 28 wherein the first transmembrane polypeptide is an MHC class II β chain and wherein the second transmembrane polypeptide is an MHC class II α chain.

30. The composition of claim 28 wherein the first transmembrane

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polypeptide is a TCR α chain and wherein the second transmembrane polypeptide is a TCR β chain.

31. The composition of claim 28 further comprising a pharmaceutically acceptable carrier.

32. The composition of claim 28 wherein a population of the molecular complexes is bound to the cell, wherein the antigenic peptides of the population are identical.

33. A method for treating a patient suffering from an allergy, comprising:

10 administering to the patient the molecular complex of claim 1 at a dose sufficient to suppress or reduce a T cell response associated with the allergy, wherein each ligand binding site is bound to an antigenic peptide, wherein the antigenic peptide is an antigen to which the patient has an allergic response.

15 34. A method for treating a patient who has received or will receive an organ transplant, comprising:

administering to the patient the molecular complex of claim 1 at a dose sufficient to suppress or reduce an immune response to the organ transplant, wherein each ligand binding site is bound to an antigenic peptide, wherein the antigenic peptide is an alloantigen.

20 35. A method for treating a patient suffering from an autoimmune disease, comprising:

25 administering to the patient the molecular complex of claim 1 at a dose sufficient to suppress or reduce the autoimmune response, wherein each ligand binding site is bound to an antigenic peptide, wherein the antigenic peptide is one to which the patient expresses an autoimmune response.

30 36. A method for treating a patient having a tumor, comprising:

administering to the patient the molecular complex of claim 1 at a dose sufficient to induce or enhance an immune response to the tumor, wherein each ligand binding site is bound to an antigenic peptide, wherein the

antigenic peptide is expressed on the tumor.

37. A method for treating a patient having an infection caused by an infectious agent, comprising:

5 administering to the patient the molecular complex of claim 1 at a dose sufficient to induce or enhance an immune response to the infection, wherein each ligand binding site is bound to an antigenic peptide, wherein the antigenic peptide is a peptide of the infectious agent.

38. A method of labeling antigen-specific T cells, comprising:

10 contacting a sample which comprises antigen-specific T cells with the molecular complex of claim 1, wherein each ligand binding site is bound to an identical antigenic peptide, whereby the antigenic peptide specifically binds to the antigen-specific T cells, thereby labeling the cells with the molecular complex.

15 39. The method of claim 38 further comprising the step of:

separating the antigen-specific T cells which are bound to the antigenic peptides from cells which are not bound.

20 40. The method of claim 38 wherein the separated cells are treated with a reagent and reinfused into a patient.

25 41. The method of claim 39 wherein the step of separating is performed using flow cytometry.

42. The method of claim 38 further comprising the step of: counting the number of antigen-specific T cells which are bound to the antigenic peptides.

43. The method of claim 38 wherein said step of contacting is performed *in vitro*.

25 44. The method of claim 38 wherein said step of contacting is performed *in vivo*.

30 45. A method of activating antigen-specific T cells, comprising: contacting a sample which comprises antigen-specific T cells with the molecular complex of claim 1 wherein each ligand binding site of the molecular complex is bound to an antigenic peptide, whereby the antigenic

peptide specifically binds to and activates the antigen-specific T cells.

46. The method of claim 45 wherein the step of contacting is performed *in vitro*.

5 47. The method of claim 45 wherein the step of contacting is performed *in vivo*.

48. A method of labeling a specific peptide/MHC complex, comprising:

10 contacting a sample comprising a peptide/MHC complex with the molecular complex of claim 3, whereby the ligand binding site specifically binds to and labels the peptide/MHC complex.

49. The method of claim 48 wherein the step of contacting is performed *in vitro*.

50. The method of claim 48 wherein the step of contacting is performed *in vivo*.

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